PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

To:

F B RICE & CO
139 Rathdowne Street
Carlton, Victoria 3053
AUSTRALIE

NOTIFICATION CONCERNING TRANSMITTAL OF COPY OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (CHAPTER I OF THE PATENT COOPERATION TREATY)
(PCT Rule 44bis.1(c))

Date of mailing *(day/month/year)* 06 October 2005 (06.10.2005)	
Applicant's or agent's file reference 502300	**IMPORTANT NOTICE**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/AU2004/000358	22 March 2004 (22.03.2004)	21 March 2003 (21.03.2003)

Applicant
THE ROYAL ALEXANDRA HOSPITAL FOR CHILDREN et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.+41 22 740 14 35	Authorized officer Dorothée Mülhausen Facsimile No.+41 22 338 87 40

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 502300	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/AU2004/000358	International filing date *(day/month/year)* 22 March 2004 (22.03.2004)	Priority date *(day/month/year)* 21 March 2003 (21.03.2003)]
International Patent Classification (IPC) or national classification and IPC [7] A61K 31/7088, 38/00, A61P 11/00, 1/00, G01N 33/15, 33/68, 33/50, 33/53, 33/483		
Applicant THE ROYAL ALEXANDRA HOSPITAL FOR CHILDREN		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 23 September 2005 (23.09.2005)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Dorothée Mülhausen Telephone No. +41 22 338 87 40

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the:
INTERNATIONAL SEARCHING AUTHORITY

REC'D 18 MAY 2004
PCT WIPO PCT

To:

F.B. Rice & Co.
139 Rathdowne Street
CARLTON VIC 3053

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	13 MAY 2004
Applicant's or agent's file reference 502300/JEP/mpg	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/AU2004/000358	22 March 2004	21 March 2003

International Patent Classification (IPC) or both national classification and IPC
Int. Cl.[7] A61K 31/7088, 38/00, A61P 11/00, 1/00, G01N 33/15, 33/68, 33/50, 33/53, 33/483

Applicant
THE ROYAL ALEXANDRA HOSPITAL FOR CHILDREN et al

1. This opinion contains indications relating to the following items:

- [X] Box No. I — Basis of the opinion
- [ ] Box No. II — Priority
- [ ] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV — Lack of unity of invention
- [X] Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI — Certain documents cited
- [ ] Box No. VII — Certain defects in the international application
- [X] Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the IPEA/AU
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[redacted]

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2004/000358

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/AU2004/000358

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	**1-23, 27-43**	**YES**
	Claims	**24-26**	**NO**
Inventive step (IS)	Claims	**2, 11-18, 20-23, 27-32, 41-43**	**YES**
	Claims	**1, 3-10, 19, 24-26, 33-40**	**NO**
Industrial applicability (IA)	Claims	**1-43**	**YES**
	Claims		**NO**

2. Citations and explanations:

This opinion is based on the following documents cited in the Search Report:

D1: DUNN, S. *et al.* Hypertension (2003) 41: 347-354.

D2: LI, Q. *et al.* Journal of Molecular Biology (2003) 325: 949-962.

D3: DALBY-PAYNE, J. R. *et al.* Molecular Biology of the Cell (2003) 14: 4365-4375.

NOVELTY (N) claims 24-26

D1 discloses that an elevated TPMN/TPM5b ratio of the protein in erthyrocytes and RNA in leukocytes is correlated with abnormal Na^+/Li^+ countertransport across the cell membrane, caused by kinetic changes in the function of the Na^+/Li^+ countertransporter. The document teaches that tropomyosin modulates the sodium ion-binding affinity on the membrane exterior surface, and that Na^+/Li^+ countertransport is sensitive to tropomyosin influences on the cytoskeleton demonstrated by a change in Na^+/Li^+ countertransport kinetics occurs with liposome-delivered tropomyosin antibodies. A role for gene polymorphisms in the pathogenesis of essential hypertension with abnormal Na^+/Li^+ countertransport was proposed. (See Abstract, page 348 1st para, page 353 left column 2nd para and Perspectives, and Fig 5). The disclosure of this document anticipates the invention of claims 24-26, rendering it not novel.

Continued in Supplemental box

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2004/000358

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-43 are not supported by the description insofar as these claims encompass the activity of *any* cell surface protein with *any* tropomyosin isoform. The invention appears to arise from the finding of an association between tropomyosins 5a and 5b with the cell surface protein cystic fibrosis transmembrane conductance regulator (CFTR). The applicant has not described the association of other tropomyosin isoforms with this protein, in fact several are shown not to do so, and the applicant admits on page 56 lines 2-3 that tropomyosin isoforms have different functions. Therefore there is no support in the description for claims having a broader scope than tropomyosin isoforms 5a and 5b and the CFTR.

Claims 20-41 are not supported by the disclosure of the specification because the 'agents that modulate tropomyosin expression' are only generically described and there is no best method of performance provided for the invention of these claims.

Claim 42 is not supported by the description because no tropomyosin gene mutations are disclosed that would affect an individual's predisposition to a disease caused by the abnormal insertion, retention or activity of a cell surface membrane protein, and therefore this claim is merely speculative.

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Box V.

INVENTIVE STEP (IS) claims 1, 3-10, 19, 24-26 and 33-40

D1 provides the closest prior art, while D2 teaches the *in vivo* association of the proteins tropomyosin-1 and polycystin-2 and the interaction of these proteins in a yeast 2-hybrid (Y2H) screen.

The technical problem addressed by claims 1-10 is considered to be the provision of methods for screening for compounds that modify the activity or cellular location of tropomyosin and thereby indirectly regulate the activity or cellular location of a cell surface protein.

Given the teaching of D1 it would be obvious to the skilled person to apply screening methods well known in the art to identify alternative compounds that modify tropomyosin activity or expression and therefore claims 1, 3 and 4 lack an inventive step.

Given the disclosure of D1, it would also be obvious to the skilled person to use the Y2H screen of D2 to identify compounds that modulate tropomyosin activity by interfering with the association of this protein to its intracellular binding partners, and therefore claims 5, 6, 9 and 10 lack an inventive step. Modification of the Y2H screen described to incorporate other known tropomyosin binding partners to arrive at the invention of claims 7 and 8 would be well within the capacity of the skilled person.

The invention defined in claims 24-26 is not inventive because the features of these claims is disclosed in D1.

Dependent claims 19 and 33-40 do not confer inventiveness on the any of the above non-inventive claims because (i) formulating an identified compound for administration to a human or animal (claim 19) would be within the common general knowledge of the skilled person, and (ii) claims 33-40 merely define tropomyosin genes and alternative types of modulatory agents, both of which are well known in the field.

In summary, claims 1, 3-10, 19, 24-26 and 33-40 lack an inventive step.

The priority of the application appears validly claimed therefore document D3, published in November 2003 before the international filing date but after the priority date of the application is not considered part of the prior art base for this application..